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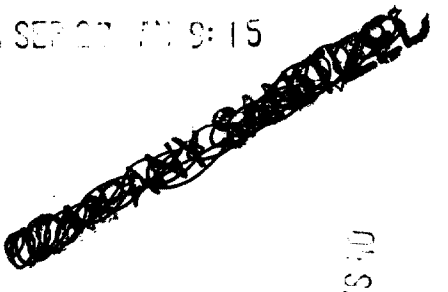
September 24, 2003



3M

By Hand Delivery

Document Processing Center (7407)
Office of Pollution, Prevention and Toxics
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N. W.
Washington, DC 20460
Attention: Section 8(e) Coordinator

CBI

Re: **TSCA Section 8(e) Submissions**

Dear Sir/Madam:

3M Company ("3M") requests that EPA place the attached studies in the TSCA Section 8(e) docket. We have included a master index for these studies identifying the study title, test substance and CAS number. A Confidential Business Information (CBI) version of this index and the studies also is being submitted today pursuant to EPA procedures. 3M has not provided CBI substantiation with this submission, but would be willing to do so at the Agency's request.

3M has concluded that data in these studies may not be, strictly speaking, "corroborative" of previously reported or published information as defined in EPA's reporting guidance or otherwise potentially may warrant 8(e) submission based on EPA's reporting guidance.

3M appreciates EPA's attention to this matter. Please contact the undersigned if you have any questions or require further information regarding this submission.

Very truly yours,

Katherine E. Reed (q.a.v.)

Dr. Katherine E. Reed, Ph.D
Staff Vice President
Environmental Technology and Safety Services
(651) 778-4331
kereed@mmm.com

Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
(Confidential Business Information Redacted)

Primary Eye Irritation Study - Rabbits	[ ]	[ ]
Guinea Pig Contact Dermal Irritation/Sensitization	20% solids (Ethomeen S/12 1.0M with diethyl sulfate 0.94M); 80% water [Ethomeen S/12 = R-N(Et)+(C2H4OH)2 where R=C18 with 1-2 double bonds]	20% (61791-24-0 with 64-67-5); 80% 7732-18-5
Primary Eye Irritation Study - Rabbits	Butanoic acid, heptafluoro-, calcium salt	2366-98-5
Acute Oral Toxicity Screen with T-2712CoC in Albino Rabbits	perfluorohexanoic acid	307-24-4
Primary Skin Irritation Test with T-2725Ec (Repeat Application) in Albino Rabbits	[ ]	[ ]
Acute Ocular Irritation Test with T-2725Ec in Albino Rabbits	[ ]	[ ]
Sensitization Study with T-2741AC in Albino Guinea Pigs	[ ]	[ ]
Oral Rangefinder Study of T-3140BS in Pregnant Rats	1-[3'-(perfluorooctanesulfonate) anilino amide]-2 potassium 3,4,5,6-tetrachlorophthalate	57589-85-2
Oral Rangefinder Study of T-3139BS in Pregnant Rats	80% 1-[3'-(perfluorooctanesulfonate) anilino amide]-2-potassium 3,4,5,6-tetrachlorophthalate; 5% C7 homolog; 5% C5 homolog; 5% C4 homolog; 5% C6 homolog	80% 57589-85-2; 5% 68541-01-5 ; 5% 68541-02-6; 5% 68568-54-7; 5% 68815-72-5
Acute Occular Irritation Test with T-2997CoC in Albino Rabbits	perfluoroethylcyclohexylsulfonic acid diethanol amine salt	salt of 133201-07-7 and 111-42-2
Sensitization Study with T-3386 in Albino Guinea Pigs	[ ]	[ ]
In Vitro Microbiological Mutagenicity Assays of 3M Company's Compound T-3411	[ ]	[ ]

COMPANY SANITIZED

Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
(Confidential Business Information Redacted)

[redacted]	[redacted]	[redacted]
Acute Oral Toxicity Screen with T-3448 in Albino Rats	68% poly(oxy-1,2-ethanediyl), alpha-[2-[ethyl[(heptanedecafluorooctyl)sulfonyl]amino]ethyl]-omega-hydroxy-; 12% polethylene glycol; 7% water; 4.86% poly(oxy-1,2-ethanediyl), alpha-[2-[ethyl[(pentadecafluoroheptyl)sulfonyl]amino]ethyl]-omega-hydroxy-; 4% residual organic fluorochemical; 3% heptadecafluoro-1-octanesulfonic acid; 0.81% poly(oxy-1,2-ethanediyl), alpha-[2-[ethyl[(undecafluoropentyl)sulfonyl]amino]ethyl]-omega-hydroxy-; 0.3% 1,4-dioxane; 0.2% n-ethylperfluorooctanesulfonamidoethyl alcohol; 0.03% linear n-ethyl perfluorooctanesulfonamide	68% 29117-08-6; 12% 25322-68-3; 7% 7732-18-5; 4.86% 56372-23-7; 4.05% 68298-79-3; 3.24% 68298-81-7; 3% 1763-23-1; 0.81% 68298-80-6; 0.3% 123-91-1; 0.2% 1691-99-2; 0.03% 4151-50-2
In Vitro Microbiological Mutagenicity Assays of 3M Company's Compound T-3516	[redacted]	[redacted]
Acute Dermal Toxicity Study with T-3451 in Albino Rabbits	C8F17SO2N(CH3).Na	Unknown
Acute Oral Toxicity - Method, Summary, Pathology; Primary Dermal Irritation - Method, Summary; Primary Eye Irritation - Method, Summary; Guinea Pig Maximization - Method, Summary	[redacted]	[redacted]
Acute Oral Toxicity - Method, Summary, Pathology; Primary Dermal Irritation - Method, Summary; Primary Eye Irritation - Method, Summary;	[redacted]	[redacted]
	[redacted]	[redacted]
Dermal Sensitization Study in Guinea Pigs, Maximization Test - Method, Summary	[redacted]	[redacted]
	[redacted]	[redacted]
4 Hour Acute Aerosol Inhalation Toxicity Study with T-3825 in Rats	[redacted]	[redacted]
Primary Eye Irritaiton/Corrosion Study in Rabbits	[redacted]	[redacted]
4-Hour Acute Aerosol Inhalation Toxicity Study with T-3825 in Rats	[redacted]	[redacted]

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T-3820: Acute Inhalation Toxicity Test	[ ]	[ ]
T-3821: Acute Inhalation Toxicity Test	[ ]	[ ]
T-3845 Acute Inhalation Toxicity Test	heptafluorobutyryl chloride	375-16-6
Evaluation of the Acute Inhalation Toxicity of T-3920 in the Rat	[ ]	[ ]
Primary Eye Irritation Study in Rabbits - Method, Summary	Decanoic acid, nonadecafluoro-, ammonium salt	3108-42-7
Acute Oral Toxicity Study in Rats (OECD Guidelines)	95% ammonium perfluorodecanoate; 5% ammonium perfluorooctanoate	5% 3825-26-1
Acute Inhalation Toxicity Study with T-4129 in the Rat	[ ]	[ ]
Acute Inhalation Toxicity Study with T-4130 in the Rat	[ ]	[ ]
Acute Oral Toxicity Study in Rats; Acute Dermal Irritation Study in Rabbits; Acute Eye Irritation Study in Rabbits	[ ]	[ ]
Dermal Sensitization Study in Guinea Pigs - Maximization Test	[ ]	[ ]
Mutagenicity Test on T- 4413 [ ] Mouse Lymphoma Forward Mutation Assay with Duplicate Cultures	[ ]	[ ]
Acute Inhalation Toxicity Study with T-4354 in the Rat	[ ]	[ ]
Primary Dermal Irritation/Corrosion Study in Rabbits	[ ]	[ ]
Acute Inhalation Toxicity Study in the Rat with T-4397	[ ]	[ ]
Primary Eye Irritation/Corrosion Study of T-5261 in Rabbits	lithium tetrafluoroethane-1,2-disulfonimide	Unknown
Acute Inhalation Toxicity Evaluation on T-5231 in Rats	[ ]	[ ]
4-Hour, Acute Inhalation Toxicity Study with T-5305 in Rats	[ ]	[ ]
4-Hour, Acute Inhalation Toxicity Study (Limit Test) with T-5343.1 in Rats	[ ]	[ ]

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Title	Name of Chemical	CAS Number
4-Hour, Acute Inhalation Toxicity Study With T-5306 in Rats	[ ]	[ ]
4-Hour, Acute Inhalation Toxicity Study (Limit Test) with T-5357.1	[ ]	[ ]
Acute Dermal Toxicity Study of T-4201 in Rabbits	Lithium Bis(Trifluoromethanesulfonyl)imide	90076-65-6
SubAcute 28-Day Oral Toxicity with T-2816 by Daily Gavage in the Rat Followed by a 14 Day Recovery Period	[ ]	[ ]
Subacute 28-Day Oral Toxicity with T-2816 by Daily Gavage in the Rat Followed by a 14-Day Recovery Period	[ ]	[ ]
Acute Inhalation Toxicity Evaluation on T-5187 in Rats	[ ]	[ ]
T-4240 4-Week Oral Toxicity Study in Rats	[ ]	[ ]
Dermal Sensitization Study of T-5473 in Guinea Pigs - Maximization Test	[ ]	[ ]
4-Hour, Acute Inhalation Toxicity Study With T-5698 in Rats	[ ]	[ ]
Acute Inhalation Toxicity Evaluation On T-5708 in Rats	[ ]	[ ]
T-5486 Assessment of Cardiac Sensitization Potential in Dogs	octafluoropropane	76-19-7
Acute Inhalation Toxicity Evaluation on T-5655 in Rats	[ ]	[ ]
T-4201 4 Week Oral Toxicity Study in Rats with 2-Week Recovery Period	Lithium Bis(Trifluoromethanesulfonyl)imide	90076-65-6
T-5658: Eye Irritation to the Rabbit	[ ]	[ ]
Acute Inhalation Toxicity Evaluation on T-5715 in Rats	[ ]	[ ]
Acute Inhalation Toxicity Evaluation on T-5716 in Rats	[ ]	[ ]
Acute Inhalation Toxicity Study of T-5724 in Rats	[ ]	[ ]
Acute Inhalation Toxicity Study of T-5725 (Resin Solution) in Rats	[ ]	[ ]

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Acute Inhalation Toxicity Study (Limit Test) of T-5927 in Rats	[ ]	[ ]
Acute Inhalation Toxicity Study of T-5928 in Rats (LC50)	[ ]	[ ]
Acute Inhalation Toxicity Evaluation on T-5829 in Rats	[ ]	[ ]
Single-Dose Intravenous Pharmacokinetic Study of T-5963 in Rabbits	[ ]	[ ]
Single-Dose Intravenous Pharmacokinetic Study of T-6030 in Rabbits	[ ]	[ ]
5-Daily Dose Dermal Absorption/Toxicity Study of T-6029 and T-6032 in Rabbits	87-93% fluorinated alkyl alkoxylates; 4-10% linear N-ethyl perfluorooctanesulfonamide; 2-4% poly(oxy-1,2-ethanediyl),.alpha.-[2-[ethyl[(pentadecafluoroheptyl)sulfonyl]amino]ethyl]-.omega.-methoxy-; 0-4% residual organic fluorochemicals; 0-2% c8 sulfonamide; 0.1-1% 1-heptanesulfonamide, N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,7-pentadecafluoro-; miscellaneous components (each less than 1%)	87-93% 68958-61-2; 4-10% 4151-50-2; 2-4% 68958-60-1; 0-2% 31506-32-8; 0.1-1% 68957-62-0
Single-Dose Intravenous Pharmacokinetic Study of T-6061 in Rabbits	[ ]	[ ]
Single-Dose Intravenous Pharmacokinetic Study of T-6065 in Rabbits	[ ]	[ ]
Single Dose Intravenous Pharmacokinetic Study of T-6063 in Rabbits	[ ]	[ ]
Acute Inhalation Toxicity Study of T-6235 in Rats	[ ]	[ ]
Primary Dermal Irritation/Corrosion Study of T-6402 in Rabbits	[ ]	[ ]
Dermal Sensitization Study of T-6402 in Guinea Pigs- Maximization Test (EC Guidelines)	[ ]	[ ]
Acute Eye Irritation/Corrosion Study with T-6318 in the Rabbit	1-Butanesulfinic acid, 1,1,2,2,3,3,4,4,4-nonafluoro-, Sodium Salt	102061-82-5

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Primary Skin Irritation / Corrosion Study with T-6567 in the Rabbit (4-Hour Semi-Occlusive Application)	[ ]	[ ]
Assessment of Contact Hypersenitivity to T-6318 in the Albino Guinea Pig (Maximization Test)	1-Butanesulfinic acid, 1,1,2,2,3,3,4,4,4-nonafluoro-, Sodium Salt	102061-82-5
Single-Dose Intravenous Pharmacokinetic Study of T-6502 in Rabbits	[ ]	[ ]
Single-Dose Intravenous Pharmacokinetic Study of T-6504 in Rabbits	[ ]	[ ]
Single Dose Intravenous Pharmacokinetic Study of T-6506 in Rabbits	[ ]	[ ]
A Study for Effect on Embryofoetal Development of the Rat (Inhalation Administration)	20-80% methyl nonafluoroisobutyl ether; 20-80% methyl nonfluorobutylether	20-80% 163702-08-7; 20-80% 163702-07-6
Bacterial Reverse Mutation Test of T-6695	[ ]	[ ]
5-day Inhalation Toxicity of Perfluorocyclohexene ([ ]; T-6878) in Rats	70% crude perfluorocyclohexene; 30% perfluoromethylcyclopentene	70% 355-75-9
5-Daily Dose Dermal Absorption/Toxicity Study of T-6502 and T-6503 in Rabbits	[ ]	[ ]
Primary Eye Irritation/Corrosion Study of T-6786 in Rabbits	Lithium Bis(perfluoroethylsulfonyl)imide	132843-44-8
Primary Dermal Irritation/Corrosion Study of T-6804 in Rabbits	Lithium Bis(perfluoroethylsulfonyl)imide	132843-44-8
5-Day Inhalation Toxicity Screen of HFE [ ]	c-C6F11OCH3	4943-08-2
Primary Eye Irritation/Corrosion Study of T-6804 in a Rabbit (OECD Guidelines)	Lithium Bis(perfluoroethylsulfonyl)imide	132843-44-8
Acute Oral Toxicity Study of T-6804 in Rats (OECD Guidelines)	Lithium Bis(perfluoroethylsulfonyl)imide	132843-44-8
Dermal Sensitization Study of T-6908 in Guinea Pigs, Mazimization Test (EC Guidelines)		

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Eye Irritation/Corrosion Study of T-4127 in the Rabbit	N-Me Fos Amide-Triphenylbenzyl Phosphonium Chloride Complex; D-1624	31506-32-8
Single-Dose Intravenous Pharmacokinetic Study of T-6924 in Rabbits	[ ]	[ ]
Dermal Sensitization Study of T-6924 in Guinea Pigs- Maximization Test (EC Guidelines)	[ ]	[ ]
Dermal Sensitization Study of T-7003 in Guinea Pigs - Maximization Test (EC Guidelines)	[ ]	[ ]
Report of Sera and Liver Data for [ ] Monoester - Preliminary ADME Study in Rats	N-ethyl heptadecafluoro-N[2-(phosphonooxy)ethyl] octanesulfonamide diammonium salt	67969-69-1
[ ] Diester-Pharmacokinetic Study in Rats (Study No. T-7043.1, DT-26)	ammonium bis[ethyl(perfluorooctane)sulfonayl]phosphate	30381-98-7
Single Dose Intravenous Pharmacokinetic Study with T-7082 in Rabbits	[ ]	[ ]
[ ] Monoester - Pharmacokinetic Study in Rats (Study No. T-6997.2)	N-ethyl heptadecafluoro-N[2-(phosphonooxy)ethyl] octanesulfonamide diammonium salt	67969-69-1
Determination of PFOS Presence and Concentration in Serum from the Dermal Absorption Studies of T-7106 and T-7107 in Hra:(NZW)SPF Rabbits	[ ]	[ ]
Dermal Sensitization Study of T-7285.5 in Guinea Pigs - Maximization Test (EPA/OECD Guidelines)	[ ]	[ ]
Twenty-eight Day Repeated-Dose Oral Toxicity Study of T-6861 in Rats	Lithium Bis(perfluoroethylsulfonyl)imide	132843-44-8
Twenty-eight Day Repeated Dose Oral Toxicity Study of T-7005 in Rats	[ ]	[ ]

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	potassium perfluorooctanoate	2395-00-8
Five Day Inhalation Toxicity Study of [ ] Monochloride, [ ], and HCFC225cb in Male CD Rats	C4F9-OCH2Cl	205367-42-6 (n-isomer) and 221617-86-3 (l-isomer)
	c-C6F11-CF2-O-CH3	181214-67-5
	CF2ClCF2CHClF	507-55-1
Toxicokinetic Screen of [ ] (T-7483) in Rats	C7F15C(O)N(H)CH3	89685-56-3
Low Level Oral Perfluorooctanesulfonate (PFOS) Dose Toxicokinetic Study in Rats: Serum and Liver PFOS	84% 1-octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-, potassium salt; 5.5% potassium (perfluorohexyl)sulfonate; 4% potassium nonafluorobutanesulfonate; 4% potassium perfluoroheptanesulfonate; 2% potassium perfluoropentanesulfanate; 0.5% unknown	84% 2795-39-3; 5.5% 3871-99-6; 4% 29420-49-3; 4% 60270-55-5; 2% 3872-25-1

RCC NOTOX
Research and Consulting Company b.v.

EYE IRRITATION/CORROSION STUDY OF T-4127 IN THE RABBIT

RCC NOTOX Study Ref. No. 0782/989
April, 1988

Sponsor

Medicine
Health Physics
Industrial Hygiene
Toxicology
Medical Department/3M
3M Center
St. Paul, Minnesota 55144
USA

Testing Facility

RCC NOTOX B.V.
Hambakenwetering 7
5231 DD 's-Hertogenbosch
The Netherlands
Tel: (0)73-419575
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STATEMENT OF GLP COMPLIANCE

The study was conducted in compliance with the current Good Laboratory Practice Regulations for non-clinical laboratory studies as set forth by both the US FDA (21 CFR 58) and the US EPA (40 CFR 160 and 40 CFR 792), as well as in accordance with the OECD Principles of Good Laboratory Practice.

I, the undersigned, further declare that the study reported here has been carried out according to the agreed protocol and that this report contains an accurate description of the results.

The raw data and final report relating to this study are stored in the RCC NOTOX archives for a period of 10 years. Further storage will be subject to authorization by the sponsor, who will be notified well in advance of any raw data destruction programme.

SUBMITTED BY:

Study Director

P.A.M. Daamen — April 29, 1988

Date

QUALITY ASSURANCE STATEMENT

This report has been audited by the RCC NOTOX Quality Assurance Unit. It is considered to be an accurate presentation of the procedures and practices employed during the course of the study and an accurate presentation of the findings.

The type of study described in this report is conducted virtually continuously at RCC NOTOX and involves frequent repetition of similar or identical procedures within a short time period. At or about the time the study was in progress each critical phase of this study type was inspected at least once every two months over a series of studies, as part of a comprehensive 'umbrella-inspection' schedule.

Inspection and report audit findings were reported to Management and the Study Director.

FINAL REPORT AUDITED BY:

Quality Assurance Officer

J.A. Andeweg — April 29, 1988

Date

CONTENTS

SUMMARY

A sample of T-4127 was tested in the rabbit acute eye irritation/ corrosion test.

Instillation of approximately 100 mg of the test substance in one of the eyes of each of three albino rabbits resulted in adverse effects on the cornea, iris and conjunctivae.
Approximately 60 minutes after exposure one animal showed nacreous areas of corneal opacity, two animals showed very slight corneal opacity and all three animals also showed slight conjunctival redness and moderate chemosis. All three animals showed no iris reaction to light.
The corneal opacity noted in the two animals increased to translucent areas by day 2. After day 7, a further decrease was noted, but slight corneal opacity was still observed in all three animals by day 21. All three rabbits showed injection of the iris and no reaction to light (except for animal 4481 on day 1) during the entire observation period.
The slight conjunctival redness increased to diffuse beefy red with white/grey coloured spots in all three animals during the following days. Slight redness and white/grey coloured spots were still observed in all three rabbits on day 21, when the study was terminated. The moderate chemosis noted in two animals increased to severe by the next day and decreased slowly after day 2. However, slight chemosis was still observed in one animal on day 21 and had resolved in two animals by that day.

Based on the estimated Draize score of 65.3 (day 2) the test substance should be classified as extremely irritating according to the scheme of Kay and Calandra.

According to the criteria laid down in Annex VI of the EEC Council Directive 67/548/EEC (amended by Directive 83/467/EEC), the test substance should be labelled as an eye irritant.

ASSESSMENT OF ACUTE EYE IRRITATION/CORROSION BY T-4127 IN THE RABBIT.

The purpose of the study was to evaluate the ability of the test substance to produce ocular irritation or corrosion in the rabbit eye following a single instillation.

1. GENERAL INFORMATION

1.1 Test substance

The following test substance data have been submitted by the sponsor:

- Code : T-4127
- Appearance : Solid
- Solubility : Soluble in methanol
- Storage : At room temperature in the dark
- Stability : Stable under storage conditions

1.2 Study dates

Test substance received: January 15, 1988
Initiation date : March 28, 1988
Completion date : April 18, 1988

1.3 Test Guideline

The study was carried out in conformity with EEC test method B.5, Methods for Determination of Toxicity: "Acute Toxicity - eye irritation", as described in the Annex of EEC Directive 84/449/EEC, (September 1984).

1.4 Reason for selection of the test method

The ocular route of administration is selected because the test substance may accidentally come into contact with the eyes during manufacture, handling and use. The New Zealand White rabbit is the species and strain of choice as it is readily available and easy to handle, house and treat. The absence of pigmentation of the iris facilitates the evaluation of induced eye reactions and there is a considerable amount of published literature on eye irritation available on this species to assist in the assessment of the significance of the effects observed.

1.5 Personnel

Study Director : P.A.M. Daamen
Author : P.A.M. Daamen
Study Supervisor: J.T. van Wijk

2. METHODS

2.1 Animals, diet and husbandry

Three adult female albino rabbits of the New Zealand White strain, SPF-quality, were supplied by The Broekman Institute, Someren, The Netherlands. Upon receipt, each animal was identified with an ear tag and individually housed in a plastic cage with a perforated floor. An acclimatisation period of at least five days was allowed. The animals were fed standard laboratory animal diet (100 g per day, LKK-20, diameter 4 mm), obtained from Hope Farms, Woerden, The Netherlands, and had free access to tap-water (via automatic nozzles). Certificates of analysis for both diet and drinking water are retained in the RCC NOTOX archives.
The animal room was air conditioned, with the temperature maintained within the range of 19 - 21°C and the relative humidity within the range of 50 - 85 per cent during the study. The artificial light sequence was 12 hours light, 12 hours dark.
Prior to administration of the test substance, both eyes of all animals were inspected and found to be intact and normal.

2.2 Administration of the test substance

The day of test substance administration was designated as day 0.
The test substance could not ground to a fine powder, due to its stickiness. On day of treatment, three portions of 100 ± 6 mg of the test substance were dispensed in glass containers with screw caps. Each portion of the dipensed amount of test substance was instilled in the conjunctival sac of the right eye of each animal using a spatula. The lids were then held gently together for two seconds and released. Immediately after treatment, the animals were transferred to their cages.
The left eye, remaining untreated, served as a control.

2.3 Observations

Immediately after instillation of the test substance, the animals were observed and abnormalities were recorded. In addition, the eyes were examined approximately 60 minutes, 24, 48 and 72 hours and 7, 14 and 21 days after instillation of the test substance.
Observed local (or systemic) effects other than those covered by the scoring system, were also recorded.

2.4 Grading of the ocular lesions

The following scoring system was used for grading of the ocular lesions:

CORNEA:

Opacity: degree of density (area most dense taken for reading)

No ulceration or opacity 0
Scattered or diffuse areas of opacity (other than slight dulling of normal lustre), details of iris clearly visible 1
Easily discernible translucent areas, details of iris slightly obscured 2
Nacreous areas, no details of iris visible, size of pupil barely discernible 3
Opaque cornea, iris not discernible through the opacity 4

IRIS:
Normal 0
Markedly deepened rugae, congestion, swelling, moderate circumcorneal hyperaemia or injection, any of these or any combination thereof, iris still reacting to light (sluggish reaction is positive)..... 1
No reaction to light, haemorrhage, gross destruction (any or all of these)..... 2

CONJUNCTIVAE:
Redness: (refers to palpebral and bulbar conjunctivae, excluding cornea and iris)
Blood vessels normal 0
Some blood vessels definitely hyperaemic or injected 1
Diffuse, crimson colour, individual vessels not easily discernible 2
Diffuse beefy red 3
Chemosis: lids and/or nictating membranes
No swelling 0
Any swelling above normal (includes nictating membranes) 1
Obvious swelling with partial eversion of lids 2
Swelling with lids about half closed 3
Swelling with lids more than half closed 4

2.5 Interpretation of the results

The test results were evaluated according to the EEC general classification and labelling requirements for dangerous substances (Annex VI of the EEC Council Directive 67/548/EEC as amended by Directive 83/467/EEC, September 1983).
The results of the study were also expressed as an approximate Draize score (J. Pharmacol. Exp. Ther. 82, 1944). This score was calculated with the following formula: (5 * corneal opacity grade * area of opacity grade) + (5 * iridial injury grade) + 2 * (conjunctival redness grade + chemosis grade + discharge grade). Due to the fact that according to the present protocol exact grades for the area of corneal opacity and for discharge were not determined, the obtained Draize score is approximate.

2.6 Fluorescein treatment

Approximately twenty-four hours after instillation of the test substance (immediately after scoring the corneal opacity and alterations of iris and conjunctivae), a solution of 2% fluorescein in water (pH adjusted to 7.0) was applied to both eyes of each animal to quantitatively examine the potential for corneal injury. The brightly green staining area indicating epithelial damage was estimated as a percentage of the total corneal area. This procedure was repeated 3, 7, 14 and 21 days after treatment.

3. RESULTS

Instillation of the test substance into one of the eyes of each of three albino rabbits affected the cornea, iris and the conjunctivae (see Table 1).
Approximately 60 minutes after exposure animal 4469 showed nacreous areas of 50% of the cornea, slight conjunctival redness, moderate chemosis and the iris did not react to light. Animals 4481 and 4583 showed very slight corneal opacity, slight conjunctival redness, moderate chemosis and the iris did not react to light. The corneal opacity noted in animal 4469 decreased to translucent areas, but extended on the whole cornea after the 24 hours observation. The corneal opacity noted in animals 4481 and 4583 increased to translucent areas. Slight corneal opacity was still observed in all three animals on day 21, when the study was terminated. Treatment of the eyes with fluorescein on days 1, 3, 7, 14 and 21 did reveal corneal epithelial damage to 100% in all three animals (except in animal 4481 on day 1). This corneal epithelial damage was still observed on all three rabbits on day 21.
All three rabbits showed iridial injection and showed no reaction to light (except for animal 4481 on day 1) during the entire study period.
The conjunctival redness noted in all three animals increased to diffuse beefy red with white/grey coloured spots (necrosis). These signs of necrosis had not resolved in any of the animals at the end of the study and all three rabbits showed slight conjunctival redness.
The moderate chemosis noted in animals 4469 and 4583 increased to severe within 24 hours after test substance instillation. After day 2, the chemosis had decreased in animals 4469 and 4583, had resolved by day 21 in animal 4469, but slight chemosis was still observed on day 21 in animal 4583. The moderate chemosis noted in animal 4481 decreased slowly and resolved between days 14 and 21.
Slight to severe lacrimation and an increased amount of discharge was observed in animal 4469 to day 14, in animal 4583 to day 7 and in animal 4481 to day 3.
No signs of systemic intoxication were observed in any of the rabbits.

4. CONCLUSION

Based on the estimated Draize score of 65.3 (day 2) the test substance should be classified as extremely irritating according to the scheme of Kay and Calandra.
According to the EEC criteria for classification and labelling of dangerous substances, the test substance should be labelled as an eye irritant.

5. PROTOCOL RELATED DEVIATION

The Study Director for this study was P.A.M. Daamen and not Dr. P.J.J.M. Weterings as noted in the original protocol.

TABLE 1. EYE IRRITATION SCORES FOR

TEST SUBSTANCE: T-4127

Rabbit no, sex and BW	Observations	Cornea opacity (0-4)	Cornea area (0-4)	Iris (0-2)	Conjunctivae redness (0-3)	Conjunctivae chemosis (0-4)	Conjunctivae discharge (0-3)	Draize total score	Fluorescence area %	Remarks
4469	60 min	3	2	2	1	3	2	52		-
	1 day	3	1	2	2	4	3	43	95	-
F	2 day	2	4	2	2	4	3	68		nictating membrane showed showed white/grey spots
	3 day	2	4	2	2	3	3	66	30	eyelids showed a white/grey colour
2628 g	7 day	2	4	2	3	2	2	64	100	nictating membrane showed a white/grey colour
	14 day	2	1	2	3	1	2	32	30	nictating membrane and lower eyelids showed a white/grey colour
	21 day	1	1	2	3	0	0	21	5	nictating membrane and lower eyelids showed a white/grey colour, rest showed slight redness
4481	60 min	0	4	2	1	3	2	22		cornea showed very slight opacity
	1 day	1	4	1	2	3	2	39	0	-
F	2 day	2	4	2	2	2	1	60		-
	3 day	2	4	2	2	2	1	60	100	nictating membrane showed white/grey spots
2989 g	7 day	2	4	2	3	2	0	60	100	-
	14 day	1	1	2	3	1	0	23	100	nictating membrane showed a white/grey colour
	21 day	1	1	2	3	0	0	21	30	nictating membrane showed a white/grey colour, rest showed slight redness
4583	60 min	0	4	2	1	3	3	24		cornea showed very slight opacity
	1 day	1	4	2	2	4	3	48	30	-
F	2 day	2	4	2	2	4	3	68		nictating membrane showed white/grey spots
	3 day	2	4	2	3	3	3	68	100	redness score 3 only for nictating membrane
2542 g	7 day	2	4	2	3	2	1	62	100	nictating membrane showed a white/grey colour
	14 day	1	4	2	3	1	0	38	100	eyelids showed a white/grey colour
	21 day	1	2	2	3	1	0	28	80	eyelids and lower nictating membrane showed a white/grey colour, rest showed slight redness

TABLE 2. INTERPRETATION OF THE EYE IRRITATION

TEST SUBSTANCE: T-4127

Animal no.		60 min.	1 day	2 day	3 day	7 day	14 day	21 day
4469	Cornea	30	15	40	40	40	10	5
	Iris	10	10	10	10	10	10	10
	Conjunctivae	12	18	18	16	14	12	6
	Subtotal	52	43	68	66	64	32	21
4481	Cornea	0	20	40	40	40	5	5
	Iris	10	5	10	10	10	10	10
	Conjunctivae	12	14	10	10	10	8	6
	Subtotal	22	39	60	60	60	23	21
4583	Cornea	0	20	40	40	40	20	10
	Iris	10	10	10	10	10	10	10
	Conjunctivae	14	18	18	18	12	8	8
	Subtotal	24	48	68	68	62	38	28
	Total	98	130	196	194	186	93	70
	Mean total	32.7	43.3	65.3	64.7	62.0	31.0	23.3

Kay and Calandra classification: 65.3 (day 2) with final rating as extremely irritating.